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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,871	12/13/2004	Marnix L Bosch	020093-002810US	1335

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EXAMINER	
DRODGE, JOSEPH W	
ART UNIT	**PAPER NUMBER**
1723	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,871	BOSCH ET AL.	
	Examiner	Art Unit	
	Joseph W. Drodge	1723	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☑ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *052007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 40 and 60-69 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-26 of copending Application No. 10/992,154. Although the conflicting claims are not identical, they are not patentably distinct from each other because they commonly comprise methods of using cross-flow membrane filtration to enrich recirculating solutions in leukocytes so as to culture stem cell populations.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Castino patent 4,420,398. Castino et al discloses a method and system for separating leukocytes from blood sources originally obtained as whole blood samples from human patients or donors. The blood is introduced into cross-flow membrane-containing remover units 11 and 21 through respective inlets where leukocytes are selectively removed from other blood components and constitutents to form cell populations that are enriched for leukocytes. The respective retentate populations are continuously recirculated to cell populations enriched in forms of leukocytes ("production broth" and CPAS reservoir, respectively. For claims 26-32, the cell populations are prepared by upstream filtration or leukophoresis, the blood constituents naturally contain plasma,

platelets, erythrocytes, etc. and the recycling of stream volumes may be carried out indefinitely (column 14, lines 45-50).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10,12,14,33,40-48 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castino in view of Gsell et al patent 5,695,563. Castino et al

discloses a method and system for separating leukocytes from blood sources originally obtained as whole blood samples from human patients or donors. The blood is introduced into cross-flow membrane-containing remover units 11 and 21 through respective inlets where leukocytes are selectively removed from other blood components and constitutents to form cell populations that are enriched for leukocytes. The respective retentate populations are continuously recirculated to cell populations enriched in forms of leukocytes ("production broth" and CPAS reservoir, respectively. For dependent claims, Castino also disclose the following: the cell populations being prepared by samples upstream filtration or leukophoresis , the blood constituents naturally contain plasma, platelets, erythrocytes, etc. and the recycling of stream volumes may be carried out indefinitely (column 14, lines 45-50),[claims 42-47]. Castino further discloses means for heating to controlled temperature and control of filtration flow rates [claim 2], filter pore size of about 3-5 microns or adapted to retain leukocytes [claims 3,4,41,46,47], blood sources [claims 5,6], recovery unit and crossflow filters being in loop format and connected by inlets and outlets to the units (figures, [for claims 7-10,49 and 50], means for culturing [claims 14].

These claims all differ in requiring that the inlet be disposed to introduce the blood parallel to, or tangential to the surface of the filter and the outlet being centrally disposed, and/or by requiring a vortex motion. However, Gsell teaches or infers such arrangement of inlets and outlets by illustrations in figures 1-7 and by discussion of spiral flow or vortex motion (column, lines). It would have been obvious to one of ordinary skill in the art to have constructed the filtration cells of Castino to have the

tangential inlet, vortex/spiral flow and central outlets of Gsell, so as to minimize stresses to the various types of cells in the blood being separated, and increase separation efficiency by causing flow of the blood over a larger surface area of filter surface during processing.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Castino in view of Gsell et al patent 5,695,563 as applied to claims 1-10 above, and further in view of Raehse et al patent 4,751,003 or Harm et al patent 4,722,902. Claim 11 additionally requires the crossflow chamber to be cylindrical. Both Raehse and Harm (figures, etc. show such cylindrical filter membranes for crossflow separation of blood components. It would have been also obvious to have utilized cylindrical filter membranes of Raehse or Harm also to enhance separation efficiency, since crossflow in such blood separations has been shown to result in near 100% separation rates (Abstract of Raehse).

Claims 13,15-22,34-39,49-59 and 61-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castino in view of Gsell et al patent 5,695,563 as applied to claims 1-10,12,14,33,40-48 and 60 above, and further in view of Kopf patent 6,214,221 and/or Yamanishi et al publication US2003/0134416 (patent 6,949,355), based on provisional applications 60/394,517; 60/348,228 and 60/328,724, filed on 7/9/2002; 10/29/2001 and 10/11/2001, respectively.

These claims differ in additionally requiring various means and method steps to enhance culturing of and growth of the concentrated leukocytes or substances being

derived therefrom, including beads, cell-adhering substrate and screen, tissue culture vessel to receive mature cell cultures, separate mature from immature cell cultures, temperature control means, and wash and drain lines.

Yamanishi teaches such cell culture media substrates and cell culturing and maturing method steps and system components (paragraphs 48,71,94,96,131-139 and 148 of the PGPUBS Publication). The patent teaches use of beads (column 7, lines 50-67), washing and draining means (column 5, lines 53-column 6, line 12), antigen/antibody binding substances and substrates (column 8, lines 5-38), culture of stem cells (column 9, lines 57-67), separation of mature from immature cells (column 11, lines 20-49).

Yamanishi teaches such cell culture media substrates and cell culturing and maturing method steps and system components (paragraphs 48,71,94,96,131-139 and 148 of the PGPUBS Publication). The patent teaches use of beads (column 7, lines 50-67), washing and draining means (column 5, lines 53-column 6, line 12), antigen/antibody binding substances and substrates (column 8, lines 5-38), culture of stem cells (column 9, lines 57-67), separation of mature from immature cells (column 11, lines 20-49).

Kopf teaches usuch cell culture media substrates and cell culturing and maturing method steps and system components (column 7, lines 50-67), washing and draining means (column 10, lines 47-50), antigen/antibody binding substances and substrates (column 9, lines 35-53), culture growth, nurturing \ and derivation of populations of cells (column 14, lines 35-40), separation of mature from immature cells (column 11, lines

20-49). The patent teaches use of beads (column 12, lines 25-35), separation of mature from immature cells (column 11, lines 20-49), and temperature control (column 13, lines 37-47).

It would have also been obvious to have augmented the crossflow filtration loop and recycling system and method of Castino, with the various means to culture leukocyte-derived substances and cells and stem cells, as suggested by Yaminishi or Kopf, so as to both enrich leukocyte-product cell populations and promote growth and maturing of cell cultures, so as to have a complete cell growth and culturing system in one convenient and central location, to avoid loss of cell populations and leukocyte ingredients that would otherwise result were transport of cell cultures between processing facilities.

Claims 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castino in view of Gsell et al patent 5,695,563 and Krasnoff et al patent 5,690,815. Castino et al discloses a method and system for separating leukocytes from blood sources originally obtained as whole blood samples from human patients or donors. The blood is introduced into cross-flow membrane-containing remover units 11 and 21 through respective inlets where leukocytes are selectively removed from other blood components and constitutents to form cell populations that are enriched for leukocytes. The respective retentate populations are continuously recirculated to cell populations enriched in forms of leukocytes ("production broth" and CPAS reservoir, respectively.

For dependent claims, Castino also disclose the following: the cell populations being prepared by samples upstream filtration or leukophoresis , the blood constituents naturally contain plasma, platelets, erythrocytes, etc. and the recycling of stream volumes may be carried out indefinitely (column 14, lines 45-50),[claims 42-47]. Castino further discloses means for heating to controlled temperature and control of filtration flow rates [claim 2], filter pore size of about 3-5 microns or adapted to retain leukocytes [claims 3,4,41,46,47], blood sources [claims 5,6], recovery unit and crossflow filters being in loop format and connected by inlets and outlets to the units (figures, [for claims 7-10,49 and 50], means for culturing [claims 14].

These claims all differ in requiring that the inlet be disposed to introduce the blood parallel to, or tangential to the surface of the filter and the outlet being centrally disposed, and/or by requiring a vortex motion. However, Gsell teaches or infers such arrangement of inlets and outlets by illustrations in figures 1-7 and by discussion of spiral flow or vortex motion (column, lines). It would have been obvious to one of ordinary skill in the art to have constructed the filtration cells of Castino to have the tangential inlet, vortex/spiral flow and central outlets of Gsell, so as to minimize stresses to the various types of cells in the blood being separated, and increase separation efficiency by causing flow of the blood over a larger surface area of filter surface during processing.

These claims additionally differ in requiring that the the inlet and retentate be disposed in an upper chamber above the filter surface. Krasnoff teaches such orientation in column 9, lines 1-40. It would have been an obvious expedient to have

oriented the system of Castino/Gsell vertically as shown in Krasnoff to facilitate system setup and in working rooms of laboratories and industrial settings.

Claims 61-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castino in view of Gsell et al patent 5,695,563 as applied to claims 1-10,12,14,33,40-48 and 60 above, and further in view of Yamanishi et al patent US2003/0134416 (patent 6,949,355), based on provisional applications 60/394,517; 60/348,228 and 60/328,724, filed on 7/9/2002; 10/29/2001 and 10/11/2001, respectively.

These claims differ in additionally requiring various means and method steps to enhance culturing of and growth of the concentrated leukocytes or substances being derived therefrom, including beads, cell-adhering substrate and screen, tissue culture vessel to receive mature cell cultures, separate mature from immature cell cultures, temperature control means, and wash and drain lines.

Yamanishi teaches such cell culture media substrates and cell culturing and maturing method steps and system components (paragraphs 48,71,94,96,131-139 and 148 of the PGPUBS Publication). The patent teaches use of beads (column 7, lines 50-67), washing and draining means (column 5, lines 53-column 6, line 12), antigen/antibody binding substances and substrates (column 8, lines 5-38), culture of stem cells (column 9, lines 57-67), separation of mature from immature cells (column 11, lines 20-49). It would have also been obvious to have augmented the crossflow filtration loop and recycling system and method of Castino, with the various means to culture leukocyte-derived substances and cells and stem cells, as suggested by Yaminishi, so as to both enrich leukocyte-product cell populations and promote growth

and maturing of cell cultures, so as to have a complete cell growth and culturing system in one convenient and central location, to avoid loss of cell populations and leukocyte ingredients that would otherwise result were transport of cell cultures between processing facilities.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Drodge at telephone number 571-272-1140. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Roy Sample, can reached at 571-272-1376. The fax phone number for the examining group where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either private PAIR or Public PAIR, and through Private PAIR only for unpublished applications. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JWD

July 21, 2007